

PEOPLE & IDEAS

Gaia Pigino: Inside the cell

Lucia Morgado-Palacin

Gaia Pigino studies the molecular mechanisms and principles of self-organization in cilia using 3D cryo-EM.

Gaia Pigino was only 3 yr old when she became fascinated with nature in the beautiful countryside of Siena, Italy, where she grew up. The neighbor's daughter showed her a hen in the chicken coop, and they caught it in the act of laying an egg. Gaia remembers, "This was for me almost a shock, as my experience about eggs was that they come directly out of paper boxes!" Her father was also an important part of awakening Gaia's curiosity for the amazing things in nature. He used to bring home the award-winning magazine *Airone*, the Italian equivalent of *National Geographic*. Gaia never missed an issue; even before learning to read, she could spend hours looking at the captivating photos of the wildlife. She wanted to understand what she was seeing, and maybe because of that, she was determined to do science.

Gaia took her first "scientific" steps with Professor Fabio Bernini and Professor Claudio Leonzio at the University of Siena, where she studied bioindicators of soil contamination and detoxification strategies of soil arthropods as part of her PhD project. But it was later, when she joined the laboratory of Professor Pietro Lupetti and met Professor Joel Rosenbaum, a pioneer of cilia research, that Gaia discovered the world of 3D EM and felt her place was "inside a single cell." She solidified her interest in the structure of protein complexes of cilia and flagella and boosted her passion for cryo-electron tomography (ET) in the laboratory of Professor Takashi Ishikawa, first at the ETH Zurich and then at the Paul Scherrer Institut in Switzerland. In 2012, Gaia started her own laboratory at the Max Planck Institute of Molecular Cell Biology

and Genetics in Dresden, Germany, with the vision of creating a truly interdisciplinary laboratory. Her team combines techniques from different fields such as biophysics, cell biology, and structural biology to answer open questions in the cilia field. Gaia recently moved countries again—this time to take over the position of Associate Head of the Structural Biology Research Centre, at the Human Technopole, Milan, Italy.

We reached out to Gaia to learn more about her scientific journey and future research directions.

What interested you about cilia?

The first thing that attracted me toward cilia and flagella were some EM micrographs, by Professor Romano Dallai in Siena, that showed the beautiful geometrical microtubular structures of sperm flagella. I was intrigued by the apparent perfection of these organelles that clearly showed me that a cell is a coordinated system of complex molecular machines, the mechanism of many of which we do not understand. Soon after, Professor Joel Rosenbaum introduced me to the bidirectional transport of components inside cilia, which, he explained to me, is required for both assembly and function of virtually all cilia and flagella, from the motile cilia in our lungs to the primary cilium in our kidneys. He called it intraflagellar transport (IFT) and compared it to a Pater-noster elevator, where the individual cabins were what we now call IFT trains. I was completely fascinated by the IFT system, the structure, the function, the dynamics, and the mechanism of which were still largely unknown. Quickly, I realized that in addition to IFT, cilia represent a virtually infinite



Gaia Pigino. Photo courtesy of Human Technopole.

source of open biological questions waiting to be solved, from the mechanics and regulation of the beating to the sensory function of primary cilia, and their importance for human health.

What are some of the scientific questions currently of interest in your laboratory?

In the past few years, we have made substantial contributions to the current understanding of the structure and the mechanism of the IFT (1, 2, 3). Currently, we are investigating how the structure of IFT trains relates to their functions by looking, in cryo-electron

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A young Gaia Pigino (3 yr old) the day she discovered how eggs are made. Photo courtesy of Giancarlo Pigino.

tomography, at how anterograde trains transform into retrograde trains and at how different ciliary cargoes are loaded on the trains. Beside this more classical line of research, we are exploring other approaches to study IFT, for instance we have developed a method to reactivate IFT trains *in vitro* on reconstituted microtubules. We want to use this approach to investigate the behavior of IFT trains, and their motors, in experimentally controllable conditions, e.g., in the presence of only certain tubulin posttranslational modifications. We have also made interesting discoveries about the distribution of tubulin posttranslational modifications on the microtubule doublets of the axoneme and how this spatially defined tubulin code affects the function of different ciliary components. We hope we will be able to share these new “stories” with the structural and cell biology community very soon!

What kind of approach do you bring to your work?

I believe that the main reason for why science became an integral, and dominant, part of my life is because it provides infinite riddles and continuous challenges. I have always been curious about how things work in nature, but I quickly realized that learning from books didn’t satisfy me. My desire

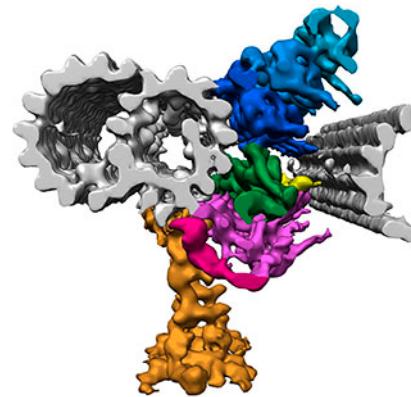
was to be at the frontline, to be among the ones that see things happening in front of their eyes, at the microscope, for the first time. I wanted to be among the ones that make the discoveries that students read about in textbooks. Thus, what I bring to my work is an endless desire of solving biological riddles, curiosity, creativity, determination, and energy, with which I hope to inspire the members of my team. My laboratory uses an interdisciplinary approach; we use whatever method, technique or technology is needed to reach our goal, from the most basic tool to the most sophisticated cryo-electron microscope. And if the method we need does not yet exist, we try to invent it.

Could you tell us a bit about the Structural Biology Research Centre at the Human Technopole (HT)?

At the HT Structural Biology Centre, we are working to create a vibrant and interdisciplinary scientific environment that will attract molecular, structural, cell, and computational biologists from all over the world. We are creating fantastic facilities, including one of the most well equipped and advanced electron microscopy facilities in Europe—and likely the world—headed by Paolo Swuec. My team, together with the teams of my colleague Alessandro Vannini and the research group leaders Ana Casañal, Francesca Coscia, and Philipp Erdmann, already cover a vast range of competences and know-how from classical molecular and structural biology approaches, such as crystallography and protein biophysics, to cryo-CLEM, cryo-FIB SEM and cryo-ET, all of which allow us to address questions in cell biology. Our goal is to create a scientific infrastructure and culture that will enable biologists to obtain a continuum of structural and functional information across scales.

What did you learn during your PhD and postdoc that helped prepare you for being a group leader? What were you unprepared for?

I learned that everyday research is mostly made of failures, but that with the right amount of obsession, persistence, curiosity, and creativity, it is always possible to succeed and discover new things. Being given the freedom to develop your own ideas and your own project very early in your career is



Structure of the 96-nm axonemal repeat reconstructed by cryo-ET and subtomogram averaging. Image courtesy of Gonzalo Alvarez Viar, Pigino Lab.

a treat; science is not only about having good ideas! One needs to follow up on these ideas with intense work and troubleshooting to make them reality. In addition, I realized that being fearless and attempting what is considered too difficult by others, despite challenges, can turn into a worthy learning experience. Also, how you present your work to the scientific community matters for swinging the odds of success in your favor. Different places might work in very different ways, and conducting good science does not only depend on you, but also on the possibilities given to you by your environment.

What was I unprepared for?—I guess several things, but one comes immediately to mind: I underestimated how much being responsible not only for my own life and career, but also the career of students, postdocs, and others in the laboratory, would affect me personally.

What has been the biggest accomplishment in your career so far?

This is a tricky question for me... I tend to look into the future more than celebrating the past. I fight to succeed in something, but as soon as I conquer it, I find it less of an achievement than the thing I could conquer next. Nevertheless, I am happy about the discoveries and the papers published together with my students and postdocs (1, 2, 3, 4, 5). I am extremely excited about the fact that after many years of work I am now leading an interdisciplinary laboratory, where we combine techniques from different

fields. I am also happy that three times my husband and I were able to move from one world class academic institution to the another to start exciting and fitting jobs and could still live together in the same place. We worked hard for this, but we also got lucky.

What has been the biggest challenge in your career so far?

I studied French in school; I had almost no exposure to spoken English until the end of my PhD. To avoid having to show my English insufficiencies, I did hide beside the board of my poster at the first international conference I attended in 2004! It took me a while to overcome this barrier and feel confident to express my thoughts and ideas in English.

What do you think you would be if you were not a scientist?

I had been a good fencer during my youth. I was a member of the Italian National Team between ages 14 and 19 and saw quite a bit of the world, which was cool! When my sporting career failed, due to diabetes, I was torn between art and science. I guess that in a parallel universe, I am a wildlife photographer and a potter specialized in wood kiln firing. [Gaia confesses that she misses “the amazing and addictive adrenaline rush of a good fencing match!”]

Any tips for a successful research career?

Do not compare your performances to the ones of the people at your career stage;

compare yourself with people that are already successful one level higher than you currently are at. For example, if you are a PhD student, ask yourself what in your current performance separates you from being a good postdoc—once a postdoc, what is missing to be a good PI.

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